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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT
REPELLENT A136328-B... (U) ARMY ENVIRONMENTAL HYGIENE
AGENCY ABERDEEN PROVING GROUND MD M H WEEKS ET AL.
APR 87 USAEHA-75-51-0434-87 F/G 24/3

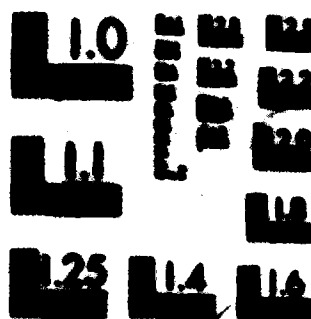
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**UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY**

ABERDEEN PROVING GROUND, MD 21010-5422

TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENT A136328-b
1-[(6-METHYL-3-CYCLOHEXEN-1-YL)CARBONYL] PYRROLIDINE
STUDY NO. 75-51-0434-87
MARCH 1987

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		PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT ACCESSION NO.
11. TITLE (Include Security Classification) Topical Hazard Evaluation Program of Candidate Insect Repellent A13-36328-b Study No. 75-51-0434-87, March 1987					
12. PERSONAL AUTHOR(S) Maurice H. Weeks and William T. Muesham					
13a. TYPE OF REPORT Final Report		13b. TIME COVERED FROM Sept 86 to Feb 87		14. DATE OF REPORT (Year, Month, Day) 87/04	
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FIELD	GROUP	SUB-GROUP			
			THEP Skin Eye Irritation		
19. ABSTRACT (Continue on reverse if necessary and identify by block number) To provide guidance for further entomological testing of the Candidate Insect Repellent A13-36328-b, 1-[(6-methyl-3-cyclohexen-1-yl) carbonyl]pyrrolidine. IRRITATION, SKIN E, TOXIC HAZARDS, TOXICITY.					
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22a. NAME OF RESPONSIBLE INDIVIDUAL Maurice H. Weeks			22b. TELEPHONE (Include Area Code) (301)571-3980		22c. OFFICE SYMBOL HSHB-MO-T



DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010-5422

REPLY TO
ATTENTION OF

MSHB-MO-T

21 April 1987

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent,
AI3-36328-b, 1-[(6-Methyl-3-cyclohexen-1-yl)carbonyl]
pyrrolidine, Study No. 75-51-0434-87, March 1987

Executive Director
Armed Forces Pest Management Board
Forest Glen Section, WRAMC
Washington, DC 20307-5001

EXECUTIVE SUMMARY

The purpose and recommendations of the enclosed report follow:

a. Purpose. To provide guidance for further entomological testing of the Candidate Insect Repellent AI3-36328-b by means of laboratory animal studies using New Zealand white rabbits. In addition, these data may be useful in developing preliminary safety guidelines for handling this compound.

b. Recommendations. Based on professional scientific judgment, the following recommendations are offered.

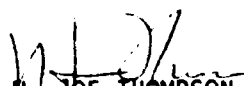
(1) AI3-36328-b should be disapproved for further extensive entomological and toxicological testing.

(2) If chemical AI3-36328-b is accidentally introduced into the eyes, they should be flushed immediately with copious amounts of water.

(3) If efficacy data is felt to warrant further entomological studies of this chemical, it should be resubmitted in a repurified form and/or at the intended use concentration.

FOR THE COMMANDER:

Encl


N. JOE THOMPSON
Colonel, MC
Director, Occupational and
Environmental Health

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HQDA(DASG-PSP-E) (w/encl)
Dir, Advisory Cen on TOX, NRC (2 cy) (w/encl)
Comdt, AHS (HSHA-IPM) (w/encl)
USDA, ARS (Dr. Terrence McGovern)(w/encl)
USDA, ARS-Southern Region (3 cy) (w/encl)
USDA, ARS-Southern Region (COL Moussa) (w/encl)
Cdr, USAMRDC (SGRD-DPM) (COL Reinert) (w/encl)

Topical Hazard Eval Program Study No. 75-51-0434-87, March 1987

d. Letter, USAEHA, HSE-LT/WP, 18 July 1980, subject: Topical Hazard Evaluation Program of Candidate Insect Repellents AI3-36325, 1-(cyclohexyl carbonyl) hexahydro-1H-azepine, AI3-36326, N,N-dipropyl-cyclohexane carboxamide, and AI3-36328, 1-[(6-methyl-3-cyclohexen-1-yl) carbonyl] pyrrolidine, Study Nos. 75-51-0833-80, 75-51-0834-80, 75-51-0835-80, October 1975 - April 1980.

3. PURPOSE. To provide guidance for further entomological testing of the Candidate Insect Repellent AI3-36328-b.

4. MATERIALS AND METHODS. *†

a. Testing for primary skin irritation and primary eye irritation was conducted using New Zealand white rabbits from Hazleton-Dutchland Laboratories, Denver, Pennsylvania.

b. The sample tested in these studies was synthesized by Dr. Terrence P. McGovern, Organic Chemical Synthesis Laboratory, USDA, Beltsville, Maryland.

c. Primary skin and eye irritation studies were performed as described in reference 2b on subject chemical.

5. SUMMARY OF FINDINGS. A tabular presentation of animal toxicity data developed by this Agency on the candidate insect repellent AI3-36328-b is shown in the Table.

6. DISCUSSION. Previous studies have shown that this compound produced only mild primary skin irritation and that it was not a photoskin irritant or a potential sensitizer (ref 2d). Although these studies also showed moderate irritation to corneal tissues at 24 hours they did not report the results of resolution at 7 and 21 days. In the present study AI3-36328-b produced mild primary irritation to the skin of rabbits as a technical grade compound and as a 25 percent ethanol solution (Appendix A, Category II). It also caused severe injury to the cornea of rabbit eyes developing into ulceration and vasculization (Appendix A, Category F). Caution should be exercised should this chemical ever be tested further.

* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education and Welfare Publication No. (NIH) 85-23, 1985.

† The studies reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

Topical Hazard Eval Program Study No. 75-51-0434-87, March 1987

TABLE. PRESENTATION OF DATA


Test	Results	Interpretation
<u>SKIN IRRITATION STUDIES</u>		
<u>Rabbits</u>		
Single 24-hour application to intact and abraded skin of New Zealand White rabbits	Chemical AI3-36328-b, produced mild primary skin irritation of the intact skin and the skin surrounding an abrasion.	USAEHA Category II (ref App A)
0.5 mL technical grade chemical applied to each of six rabbits.		
0.5 mL of a 25% (w/v) ethanol solution applied to each of six rabbits.	Chemical AI3-36328-b produced mild to moderate primary skin irritation of the intact skin of rabbits. Irritation had resolved 3 days after application.	USAEHA Category II (ref App A)
<u>EYE IRRITATION STUDIES</u>		
<u>Rabbits</u>		
Single 24-hour application of 0.1 mL technical grade chemical to one eye of each of nine New Zealand White rabbits. Three of the nine rabbits had the eye flushed with warm water for 1 minute, 25 seconds after application.	Chemical AI3-36328-b, produced pathological changes to the cornea, i.e. corneal ulceration with vascularization was observed after 14 and 21 days.	USAEHA Category B (ref Appendix A) To be used with extreme caution around the eyes and mucose. Keep away from all ocular areas.

Topical Hazard Eval Program Study No. 75-51-0434-87, March 1987

7. RECOMMENDATIONS. Based on professional scientific judgment, the following recommendations are offered. Recommend chemical AI3-36328-b be disapproved for further entomological and toxicological studies. If efficacy data of this chemical warrants further study, it should be resubmitted in a further purified form and/or at the intended use concentration.



MAURICE H. WEEKS
Chief, Toxicology Division



WILLIAM T. MUEHSAM
SGT, USA
Animal Care Specialist

APPENDIX A

TOPICAL HAZARD EVALUATION PROGRAM
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING
CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound or compounds producing necrosis, vesiculation, or eschars. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa (e.g., nose and mouth).

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D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.

APPENDIX B

ANALYTICAL QUALITY ASSURANCE

The Analytical Quality Assurance Office certifies the following with regard to this study:

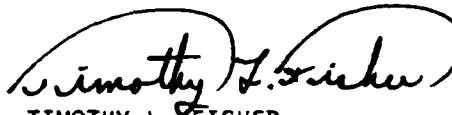
a. This study was conducted in accordance with:

(1) Standing Operating Procedures developed by the Toxicology Division, USAEHA.

(2) Title 21, Code of Federal Regulations (CFR), 1986 rev, Part 58, Good Laboratory Practice for Nonclinical Laboratory Studies.

b. Facilities were inspected during its operational phase to ensure compliance with paragraph a, above.

c. The information presented in this report accurately reflects the raw data generated during the course of conducting the study.


TIMOTHY L. FISHER
Chief, Analytical Quality
Assurance Office

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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT

REPELLENT A136328-B (U) ARMY ENVIRONMENTAL HYGIENE

AGENCY ABERDEEN PROVING GROUND MD M H WEEKS ET AL

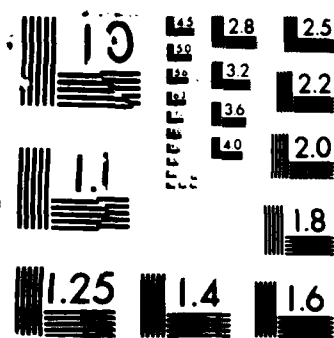
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INFORMATION



DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010-6422

REPLY TO
ATTENTION OF

4 JUN 1987

HS HB-MO-T

MEMORANDUM FOR: ADMINISTRATOR, DEFENSE TECHNICAL INFORMATION MANAGEMENT
CENTER, CAMERON STATION, ALEXANDRIA, VA 22304-6145

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent,
AI3-36328-b, 1-[(6-Methyl-3-cyclohexen-1-yl)carbonyl] pyrrolidine, Study
No. 75-51-0434-87, March 1987

The following pen and ink changes should be made to the subject report.

a. Cover Sheet, line 3, change AI36328-b to AI3-36328-b.

b. Page 3, Column 3, last entry, line 1, change USAEHA Category B to
USAEHA Category F.

FOR THE COMMANDER:

for *James R. Ciliax, LTC*
N. JOE THOMPSON
Colonel, MC
Director, Occupational and
Environmental Health

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